Short Communication

TUMOR LYSIS SYNDROME COMPLICATING TREATMENT OF WIDESPREAD METASTATIC ABDOMINAL RHABDOMYOSARCOMA

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□ *In this paper we describe a 9-year-old girl with abdominal embryonal rhabdomyosarcoma. She had ascites and widespread metastatic disease at presentation and was oliguric but had a normal creatinine. Following the start of chemotherapy she developed acute renal failure secondary to the tumor lysis syndrome, requiring hemodialysis, and had considerable myelotoxicity.*

KEY WORDS: tumor lysis syndrome, rhabdomyosarcoma, metabolic emergencies, metastatic malignancies.

Tumor lysis syndrome (TLS) is a common complication of chemotherapy in high count acute leukemia or widespread non-Hodgkins lymphoma. It is not commonly seen in association with treatment of solid tumors.

We report a case of tumor lysis syndrome associated with the treatment of widespread metastatic rhabdomyosarcoma of the embryonal histological type.

HISTORY

A 9-year-old girl was admitted with a 3-month history of intermittent abdominal and left shoulder tip pain. She gave a 1-week history of shortness of breath, increasing malaise anorexia, and abdominal distension.

On examination she was cachectic and tachypneic with dullness and reduced air entry over the left lower chest. She had tense ascites and a mass in the left hypochondrium. She was normotensive.

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INVESTIGATIONS

CT scan of her abdomen and pelvis showed extensive ascites. There were widespread peritoneal tumor deposits with infiltration of the omentum in the form of thick omental cake (Figure 1). There was also a large mass separate and more heterogenous between the spleen and the liver, displacing the gastric fundus medially. CT scan of her chest revealed two left-sided pulmonary metastases and a small left-sided pleural effusion. Bone marrow examination was normal. She underwent a percutaneous needle biopsy of the omental cake at the time of the CT scans. The histology confirmed the diagnosis of an embryonal rhabdomyosarcoma.

Treatment and Progress

Treatment was started with Carboplatin 150 mg/m^2, Epirubicin 150 mg/m^2, and vincristine 1.5 mg/m^2, according to the UKCCSG/SIOP Protocol for stage 4 malignant mesenchymal tumors.

The patient rapidly deteriorated with increasing ascites and oliguria. She became profoundly hyponatremic with a sodium level of 123 mmol/L, although the creatinine and urea were initially normal. Within 48 hours she became anuric and her urea and creatinine rose steeply, the latter to a peak of 530 μmol/L by day 9. The uric acid and phosphate rose and peaked at 72 hours to 2.1 mmol/L and 4 mmol/L, respectively. At the same time the calcium dropped to a trough of 1.5 mmol/L (Figure 2). These findings indicate that she had TLS that caused acute renal failure. She required dialysis on days 4, 5, 7, 9, and 11 following the start of chemotherapy. She began to pass urine on day 13 and required no further dialysis.

She developed severe myelosuppression, which lasted 15 days and was complicated by staphylococcal and streptococcal wound sepsis at an abdominal paracentesis site, *Escherichia coli* urinary tract infection, and interstitial pneumonitis of unknown cause, treated with high-dose septrin and steroids. She had several profound gastrointestinal hemorrhages as a complication of severe mucositis and thrombocytopaenia. Despite these serious complications, she survived. However, her renal function remained poor, and 6 months after beginning treatment, her glomerular filtration rate remained low at 46 mL/min/1.73 m^2, and she continued to have a tubular leak of potassium, phosphate, and magnesium, requiring supplementation.

There was a good response to chemotherapy, and within 6 weeks, her lung metastasis had disappeared as had most of the omental cake. She was left with a 13-cm cystic mass in the left hypochondrium. Six months after diagnosis this residual mass was removed at surgery, along with the spleen, to which it was

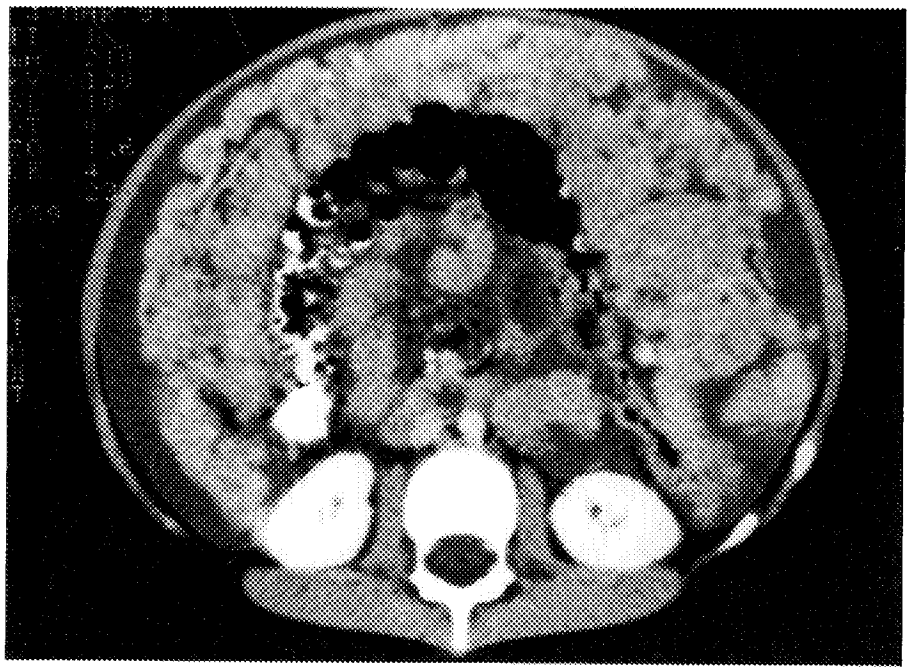

FIGURE 1. CT scan of abdomen at diagnosis. There is extensive ascites and gross induration of the greater omentum, which is infiltrated by tumor to form a thick omental cake.

adherent. No obvious residual tumor was seen at laporatomy. Histology of the mass showed no remaining viable tumor.

Nine months after the start of chemotherapy the patient was admitted with acute fulminant cardiac failure from which she died. At postmortem she was found to have cardiomyopathy with intra-mural calcification, acute tubular necrosis, and viable tumor in the left lobe of the liver. An echocardiogram post TLS had been normal, and follow-up chest x-rays for metastatic recurrence had shown no cardiac enlargement.

DISCUSSION

TLS is a recognized complication of the treatment of malignancies in which there is a large tumor burden of rapidly dividing cells, which are extremely chemosensitive.[1-3] It can lead to acute renal failure and severe metabolic derrangement and death.

Patients with high count acute lymphoblastic leukemia or non-Hodgkins lymphoma are particularly sensitive to treatment.[2,3] There have been case reports of a single dose of intrathecal methotrexate,[4] or oral steroids,[6] including single doses leading to TLS.[5] TLS in solid tumors is rare. However, there

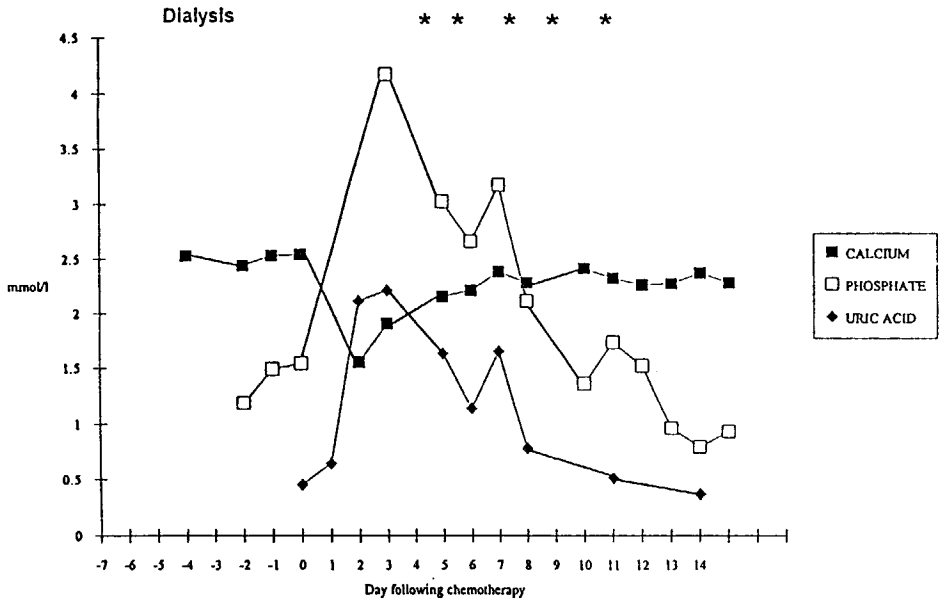

FIGURE 2. Plasma calcium, phosphate, and uric acid levels. Normal pretreatment values of calcium, phosphate, and uric acid before chemotherapy. Within 48–72 hrs of starting chemotherapy, the calcium dropped to a trough of 1.5 mmol/L (normal range: 2.2–2.6 mmol/L) with a reciprocal rise of phosphate to a peak of 4.17 mmol/L (normal range 0.8–1.4 mmol/L). There was a sharp rise of plasma uric acid levels to a peak of 2.2 mmol/L (normal range 0.12–0.45 mmol/L) in the same period. Dialysis was needed on days 4, 5, 7, 9, and 11 from the start of chemotherapy. These values began to normalize once dialysis was instituted.

are case reports in the adult literature in small cell carcinoma of the lung,[7] metastatic infiltrating ductal tumor,[8] and metastatic Meckel cell carcinoma.[9]

There has been as yet no report of rhabdomyosarcoma causing TLS because cell destruction by chemotherapy in this type of tumor is not usually as dramatic as in acute leukemia or non-Hodgkins lymphoma. However, in our case there was evidence of massive widespread abdominal disease as well as pulmonary metastases. There were both pleural and peritoneal collections of fluid, and it is possible that chemotherapeutic agents leaked into these cavities, causing increased cell kill.

Additionally, the widespread peritoneal seeding and gross ascites indicated that the biological behavior of this tumor was unusual and might indicate that it was aggressive with a high growth fraction and thus more sensitive to chemotherapy than less aggressive more slowly growing rhabdomyosarcomas. Once the diagnosis was confirmed and treatment was started, her urine output decreased over the first 24 hours and she was anuric within 48 hours. She developed acute renal failure secondary to TLS. A consequence of the acute renal failure was the probable delayed excretion of carboplatin and Epirubi-

cin, leading to more tumor destruction and was responsible for the severe mucositis and prolonged bone marrow suppression that she developed.

It is also postulated that significant cardiotoxicity occurred at the start of treatment due to the accumulation of Epuribicin in ascites and pleural effusion and as a consequence of the renal failure. The total dose of Epuribicin received was 600 mg/m^2, less than the median dose for cardiotoxicity of 850 mg/m^2 observed by Young et al.[10] We conclude that TLS should be considered in all solid tumors where there is widespread disease with features suggesting a rapidly progressing tumor and pretreatment precautions taken to prevent it.

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